b.) Remarks

Claim 1 has been amended to recite the present invention with the specificity required by statute. For the Examiner's convenience, the subject matter of the amendment may be found in the specification from page 17, line 8 to page 18, line 14, in particular page 18, line 12. Accordingly, no new matter has been added.

The Examiner objects to the language of claim 5 for the reasons noted at page 2. In response, claim 5 has above been amended in order to address the Examiner's concerns.

Claims 1-3 and 8-15 stand rejected under 35 U.S.C. §112 for lack of written description and claims 1-3 and 5-15 (sic) for lack of enablement as discussed at pages 3-9 of the Office Action. In response, solely in order to reduce the issues and expedite prosecution, the language of claim 1 has been amended in order to moot the Examiner's objection.

Claims 1-3, 6 and 8-15 remain rejected over the prior art of record. The Examiner's analyses of Nakai are found at pages 14-15 of the Advisory Action. As to that, the Examiner's conclusion that NADH-II dehydrogenase (100% identical to Applicants' SEQ ID NO: 4) isolated from *Corynebacterium glutamicum* (having 27% sequence homology to that of *E. coli*) does not function like *E. coli* NADH-II is incorrect as discussed at pages 8-9 of the December 9, 2010 Amendment. In that regard, to clarify the record Applicants provided a detailed, helpful explanation of high- and low-energy terminal oxidases and their interplay.

In response, the Examiner has neither addressed Applicants' explanation nor provided any relevant teaching of his own. To the contrary, the Examiner's analysis is

based only on the conclusory statement bridging pages 14 and 15. Respectfully submitted, this mere reiteration is not at all in conformity with MPEP §§707.07 and 707.07(f).

In any event, those skilled in this art know that protein function is defined by EC number. For instance, the EC numbers of *E. coli* NADH-II and *C. glutamicum* NADH-II are identical, namely EC:1.6.99.3 (*E. coli*: http://www.genome.jp/dbget-bin/www_bget?eco:b1109, *C. glutamicum*: http://www.genome.jp/dbget-bin/www_bget?cgb:cg1656, copies attached). Therefore, it is very well-understood that *C. glutamicum* NADH-II (Applicants' SEQ ID NO:4) has the same respiratory chain pathway function of low energy efficiency as *E. coli* NADH-II despite the low homology between them.

Additionally, contrary to the Examiner's understanding, Molennar does not teach that *C. glutamicum* only expresses type II NADH dehydrogenase. To the contrary, Molennar teach that the type II NADH dehydrogenase is, under particular conditions, the only active membrane-bound NADH dehydrogenase, wherein the specified conditions are as follows:

1. A mutant strain disrupted *ndh* gene is grown on 2 x TY medium
2. Membranes are isolated from the strain
3. NADH dehydrogenase activity is assayed DCPIP or observed NADH consumption directly by measuring the absorption at 340nm.

However, this is not material to the present invention since those persons ordinarily skilled in the art know that expression of a gene changes according to a culture conditions.

As discussed previously, because Nakai disclose that it is important in *E. coli* to be deficient of NADH-II for the production of amino acids, the present invention in which DNA encoding *C. glutamicum* NADH-II (which has the same function as *E. coli* NADH-II) is amplified, is necessarily unobvious over the prior art.

In view of the foregoing, if the Examiner is aware of some technical reasoning why Applicants' technical analysis is not to be considered persuasive as to the inapplicability of the cited art herein, he is respectfully requested to provide either (i) a reference and explanation in support of his position or (ii) a personal affidavit under MPEP §2144.03.

Entry hereof is earnestly solicited.

Applicants' undersigned attorney may be reached in our New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to our below listed address.

Respectfully submitted,

/Lawrence S. Perry/
Lawrence S. Perry
Attorney for Applicants
Registration. No. 31,865

FITZPATRICK, CELLA, HARPER & SCINTO
1290 Avenue of the Americas
New York, New York 10104-3800
Facsimile: (212) 218-2200

LSP\ac

Escherichia coli K-12 MG1655: b1109

Help

Entry	b1109 CDS E.coli
Gene name	ndh, ECK1095, JW1095
Definition	respiratory NADH dehydrogenase 2/cupric reductase (EC:1.16.1.- 1.6.99.3)
Orthology	K03885 NADH dehydrogenase [EC:1.6.99.3]
Pathway	eco00190 Oxidative phosphorylation
Class	Metabolism; Energy Metabolism; Oxidative phosphorylation [PATH:eco00190] BRITE hierarchy
SSDB	Ortholog Paralog Gene cluster GFIT
Motif	Pfam: Pyr_redox_2 Pyr_redox DAO Lycopene_cycl HI0933_like Trp_halogenase Motif
Other DBs	NCBI-GI: 16129072 NCBI-GeneID: 946792 RegulonDB: B1109 EcoGene: EG10649 ECOCYC: EG10649 UniProt: P00393
Position	1165308..1166612 Genome map
AA seq	434 aa AA seq DB search MTTPLKKIVIVGGGAGGLEMATQLGHKLGRKKKAKITLVDRNHSHLWKPLLHEVATGSLD EGVDALSYLAHARNHGFQFQLGSVIDIDREAKTITIAELRDEKGELLVPERKIAYDTLVM ALGSTSNDFNTPGVKENCIFLDNPHQARRFHQEMLNLFLKYSANLGANGKVNIAIVGGGA TGVELSAELHNAVKQLHSYGYKGLTNEALNVTLVEAGERILPALPPRISAAAHNELTKLG VRVLTQTMVTSADEGGLHTKDGEYIEADLMVWAAGIKAPDFLKDIGGLETNRINQLVVEP TLQTTRDPDIYAIGDCASCPRPEGGFVPPRAQAAHQMATCAMNNILAQMNGKPLKNYQYK DHGSLVSLSNFSTVGSLMGNLTRGSMMIEGRIARFVYISLYRMHQIALHGYFKTGLMMLV GSINRVIRPRLKLH
NT seq	1305 nt NT seq +upstream 0 nt +downstream 0 nt ttgaotaogooattgaaaaagattgtgattgtoggoggoggtgotggtgggotggaaatg gcaaocacgotggggoataagotgggacgcaagaaaaaagocaaaattaogotggtogat cgtaaccacagocacotgtggaaaoogotgotgoaogaagtggogaotggotogottgat gaaggogtogatgogttgagotatotggcccatgcgcgcaatcatggtttccagttccag otgggttccgtcattgatattgatcgtgaagcgaaaacaatcactattgcagaaotgogo gacgagaaaggtgaactgctggttccggaaogtaaaatogootatgaoaoootggtaatg gcgctgggtagoaoctotaaogatttoaataogcoaggtgtoaaagagaactgcattttc otogataaoocgoaocaggcgcgtogcttccaccaggagatgctgaatttgttcctgaaa tactccgccaacctgggcgcgaatggcaaagtgaacattgcgattgtoggoggcggcgog acgggtgtagaactctccgctgaattgcaoaagcggtoaagcaaotgoaoagotaoggt tacaaaggoctgaooaaogaagoootgaacgtaacgctggtagaagcgggagaacgtatt ttgoctgogttaoogcoacgtatctctgctgcggcccacaacgagctaacgaaaottggo gttcgcgtgctgacgcaaaccatggtcaccagtgotgatgaaggoggcotgcaoaotaaa gatggcgaatatattgaggotgatotgatggtatgggoagcogggatoaaagcgccagac ttootgaaagatatoggtggtottgaaactaaccgtatcaaccagctggtggtggaacog acgctgcaaaccoacccgcgatccagacatttacgctattggcgaotgogogtoatgcoog cgtccggaaggggctttgttcogcogogtgotcaggotgcaoaocoagatggcgaottgc gcaatgaaoaaoattotggcgoagatgaaoggtaagcogctgaaaaattatcagtataaa gatoatggttogotggtatcgctgtcgaacttctccaccgtcggtagcctgatgggtaac ctgacgcgcggctcaatgatgattgaaggaogaattgogogotttgtatatatotogota taccgaatgcatcagattgogotgoatggttaotttaaaaccggattaatgatgctggtg gggagtattaacogogttatoogtccgcgtttgaagttgcattaa

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  - KEGG GENOME (1)
- Gene (7)
  - KEGG ORTHOLOGY (1)
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  - NCBI-GI (2)
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  - ECOGENE (1)
  - REGULONDB-ECO (1)
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  - UniProt (1)
  - RefSeq(pep) (1)
- DNA sequence (2)
  - GenBank (1)
  - EMBL (1)
- Protein domain (6)
  - Pfam (6)
- All databases (20)

KEGG Corynebacterium glutamicum ATCC 13032 (Bielefeld): cg1656

Help

Entry	cg1656 CDS C.glutamicum_B
Gene name	ndh
Definition	NADH dehydrogenase (EC:1.6.99.3)
Orthology	K03885 NADH dehydrogenase [EC:1.6.99.3]
Pathway	cgb00190 Oxidative phosphorylation
Class	Metabolism; Energy Metabolism; Oxidative phosphorylation [PATH:cgb00190] BRITE hierarchy
SSDB	Ortholog Paralog Gene cluster GFIT
Motif	Pfam: Pyr_redox_2 Pyr_redox GIDA DAO FAD_binding_3 HI0933_like FAD_binding_2 Thi4 ApbA Lycopene_cycl 3HCDH_N AlaDh_PNT_C UDPG_MGDP_dh_N Saccharop_dh NAD_binding_2 DUF1188 Fucokinase Motif
Other DBs	NCBI-GI: 62390348 NCBI-GeneID: 3345393 UniProt: Q79VG1
Position	complement(1544618..1546021) Genome map
AA seq	467 aa AA seq DB search MSVNPTRPEGGRHHVVVIGSGFGGLFAAKNLAKADVDVTLIDRTNHHLFQPLLYQVATGI LSSGEIAPSTRQILGSQENVNVIKGEVTDINVESQTVTASLGEFTRVFEYDSLVVGAGAG QSYFGNDHFAEFAPGMKSIDDALEIRARIIGAFERAEICEDPAERERLLTFVVVGAGPTG VELAGQLAEMAHRTLAGEYKNFNTNSAKIILLDGAPQVLPPFGKRLGRNAQRTLEKMGVN VRLNAMVTNVDATSVTYKTKDGEEHTIESFCKIWSAGVAASPLGKLVAEQTGVETDRAGR VMVNDDLSVGDQKNVFVVGDMMNYNNLPGVAQVAIQSGEYVAEQIEAEVEGRSNTEREAF DYFDKGSMATISRFSAVVKMGKVEVTGFIGWVLWLAVHIMFLVGFRNRFVSAISWGLNAL SRKRWNLATTRQQLHSRTTLSKFAHELEEASSDLPIELRDNQRFSGK
NT seq	1404 nt NT seq +upstream 0 nt +downstream 0 nt atgtcagttaacccaacccgcccgaaggcggccgtcaccacgtcgtcgtcatcggttct ggttttggtggccttttgctgccaagaacctggccaaggcagacgtcgatgtcactctg attgaccgcaccaaccaccaccacctcttccagccactgctgtaccaagtggcaaccggtatc ctctcctccggtgaaatcgcaccttccactcgacagatcctgggctcccaggaaaacgtc aacgtcatcaagggcgaagtcaccgacatcaacgtcgagtcccagacgtgtgaccgcctcc ctgggcgagttcaccccgcgttttgagtacgattccttggtcgttggtgctggcgcaggt cagtcctacttcggcaatgatcacttcgctgagttcgcacctggcatgaagtccatcgac gatgcaatggagattcgtgcacgcatcatcggtgctttcgagcgcgctgagatctgcgag gatccagctgagcgcgaacgcctgctcaccttcgtcgttgttggcgctggcccaaccggt gttgagcttgctggccagttggctgagatggctcaccgcaccttgctggtgagtacaag aacttcaacaccaactccgcaaagatcatcctgcttgatggtgctccacaggttcttcct ccattcggtaagcgcctaggccgcaacgcacagcgcaccctggaaaagatgggtgtcaac gttcgcctgaacgctatggtcaccaacgttgacgctaccttcggtcacctacaagaccaag gacggcgaagagcacaccatcgatatctttctgcaagatttggtccgctggtgttgcggca tccccactgggcaagctgtgccgagcagaccggtgttgagaccgaccgcgcaggccgc gtcatggttaacgatgacctgtctgttggcgatcagaagaacgttctcgttgttggcgac atgatgaactacaacaacctccctggtgttgctcaggtagcaatccagagtggtgagtac gttgctgagcagatcgaagctgaggttgaaggccgctccaacacgagcgcgaagctttc gattacttgaccaagggctccatggctaccatttccccgttctccgcagtggtgaagatg ggcaaggttgaggtcaccggcttcatcggttgggttctgtggttggctgttccacatcatg ttcctggttggcttccgcaacgtttgtctctccgcaatcagctggggcctgaacgcaatg tcccgcaagcgttggaacctggcaaccacccgccagcagctccactcacgcaccacgctg tccaagttcgctccacgagcttgaggaagcatcttctgatcttccaatcgagctgcgcgac aaccagcgtttcagcggaaagtaa

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  - NCBI-Gene (1)
  - NCBI-GI (3)
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  - UniProt (1)
  - RefSeq(pep) (1)
- DNA sequence (6)
  - GenBank (3)
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  - Pfam (17)
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